

Remarks

According to the Office Action of December 8, 2003, claims 1-49 were pending in the subject application. Upon review of the application by the undersigned after receipt of the aforementioned Office Action, it was noted that claims 1-4, 9, 11, 12, 14-40, and 43-49 were canceled by way of a preliminary amendment of July 9, 2001. Examiner Fredman was contacted to discuss the Office Action, directed to canceled claims, whereupon it was agreed that claims to the canceled, but examined, subject matter would be represented by way of this response. Accordingly, claims 1-49 have been canceled in this application and claims 50-66 are newly presented. By this Amendment, Applicants have also amended the "Related Application Data" section to indicate the patent numbers for the parent applications. Support for the new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, original claims, page 22, lines 30-34 and page 61, line 30 through page 75, line 2). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 50-66 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants note that an Information Disclosure Statement (IDS) for the subject application was mailed to the Patent Office on November 20, 2001. The Office Action Summary page did not indicate receipt and consideration of the IDS. Applicants respectfully request that the Examiner contact Applicants' undersigned representative if the IDS has not been received and considered. If the IDS has been received and considered, Applicants respectfully request that its consideration be made of record with the next Action. Attached for the Examiner's convenience is a copy of the IDS submitted to the Patent Office on November 20, 2001, including Form PTO-1449, including proof of delivery of said IDS.

Claims 1-3, 11-18, and 38 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants submit that this issue is moot in view of the cancellation of the claims; however, Applicants provide the following comments with respect to the newly presented claims. Applicants respectfully submit that the subject specification provides adequate written description of the claimed invention. It is respectfully submitted that the

specification teaches that portions of SEQ ID NO: 179 can be fused to heterologous sequences, such as the  $\beta$ -globin gene or a nickel binding polypeptide (see paragraph bridging pages 79-80). Alternatively, the specification teaches any number of fragments of SEQ ID NO: 179; *e.g.*, contiguous spans of at least 6, 8, 10, 12, 15, 20, 25, 30, 50, 100, 200, or 500 nucleotides of SEQ ID NO: 179 (see paragraph bridging pages 62-63). The specification also teaches any number of positional fragments of SEQ ID NO: 179 (see, for example, page 67, about line 16). Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Claims 1-3, 11, and 12 are rejected under 35 U.S.C. § 102(b) as anticipated by Genbank Accession No. H061164 (June 21, 1995). Claims 1-3, 11, 12, and 38 are rejected under 35 U.S.C. § 102(b) as anticipated by Genbank Accession No. R96921 (September 11, 1995) and Genbank Accession No. N39909 (January 22, 1996). As these claims are now canceled, it is respectfully submitted that these rejections are moot. Applicants also respectfully submit that the newly presented claims are not anticipated by the prior art of record. For example, the claims are drawn to contiguous spans of at least 500 nucleotides of SEQ ID NO: 179 and/or to polynucleotides that are contiguous spans that are not found in the cited prior art. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 14 and 15 are rejected under 35 U.S.C. § 103(a) as obvious over Genbank Accession No. N39909 (January 22, 1996) in view of Capecchi *et al.* (1989) and claims 16-18 are rejected under 35 U.S.C. § 103(a) as obvious over Genbank Accession No. N39909 (January 22, 1996) in view of Schena (1996). As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art in order to render an invention obvious. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). It is respectfully submitted that the subject invention fails to teach all the claim limitations and that the subject invention is not *prima facie* obvious over the references.

The Office Action indicates that Genbank Accession No. N39909 teaches polynucleotides with regions that match contiguous nucleotide spans of SEQ ID NO: 179 and that the combination of these teachings with those of Capecchi *et al.* (teaching homologous recombination to form host cells and mammals) or Schena (teaching the attachment of polynucleotides to solid supports and labeling of nucleic acids) renders these claims obvious. Applicants respectfully submit that the claimed invention is not anticipated or obvious over the cited references, regardless of whether they are taken

alone or in combination. For example, the Genbank sequences cited in the Office Action fail to anticipate or render obvious the claimed contiguous spans of nucleotides and the addition of either Capecchi *et al.* or Schena *et al.* fails to remedy this defect in the teachings. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

In order to establish a case of *prima facie* obviousness, it is incumbent upon the Patent Office to determine whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, *i.e.*, to select the claimed species or subgenus from a disclosed prior art genus. *See, e.g., In re Ochoa*, 71 F.3d 1565, 1569-70, 37 USPQ2d 1127, 1131 (Fed. Cir. 1995). In the case of the instantly claimed invention, Applicants respectfully submit that one of ordinary skill in the art would not have been motivated to select Genbank Accession No. N39909 out of the plethora of EST sequences disclosed in Genbank for combination with the teachings of Capecchi *et al.* or Schema *et al.* in the absence of the disclosure and claims of the subject application, especially since the function of the polynucleotide taught in Accession No. N39909 was unknown.

Furthermore, the Office Action fails to establish that one of ordinary skill in the art would have had a reasonable expectation of success in creating a host cell or mammal exhibiting a phenotype associated with gene with which N39909 is associated via homologous recombination. For example, it is unknown if the insertion of the gene would be lethal to a host cell or transgenic animal or if a phenotypic change would even result when the gene associated with N39909 is disrupted by homologous recombination.

Additionally, it is respectfully submitted that the Office Action has derived the required motivation to combine from the disclosure and teachings of the instant specification and claims, not from the references applied against the claims. Accordingly, it is respectfully submitted that the obviousness rejection of record has improperly utilized the disclosure of these inventors as a blueprint for piecing together the prior art to defeat patentability and the withdrawal of the rejection is respectfully requested. The case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. *See, e.g., C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)

(describing “teaching or suggestion or motivation [to combine]” as an “essential evidentiary component of an obviousness holding”); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) (“the Board must identify specifically ... the reasons one of ordinary skill in the art would have been motivated to select the references and combine them”); *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination “only by showing some objective teaching [leading to the combination]”); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion “essential” to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 U.S.P.Q. 657, 667 (Fed. Cir. 1985) (district court's conclusion of obviousness was error when it “did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination”). In the case of the obviousness rejections of record, it is submitted that there is not factual teaching, suggestion, or incentive to combine the cited references and withdrawal of the rejection is respectfully requested.

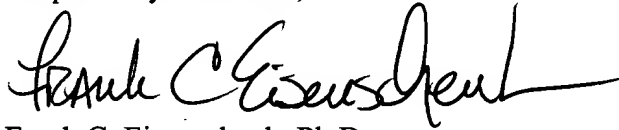
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants’ agreement with or acquiescence in the Examiner’s position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Copy of Information Disclosure Statement dated November 20, 2001